REMARKS

The amendments to the claims find support in the specification and claims as originally filed. For example, the amendments to claim 95 find support, for example, in Figure 2 and in originally filed claims 32-34; and the amendments to claim 106 find support, for example, in paragraph 11 of page 4. No new matter is added by way of the amendments. With these amendments, claims 95, 106, 108-121, 125, 128, 130, 131, and 145-163 are pending in the application.

In the Office Action Summary included with the Office Action dated September 3, 2002, the Examiner indicates that "Acknowledgement is made of applicant having filed an amendment on 20 August 2002 and on 09 October 2002 wherein the amendment of 09 October 2002 cancelled all pending claims and introduced new claims 95-166." Applicants note that the Amendment of 09 October 2002 also brought to the Examiner's attention a Preliminary Amendment and Supplemental Application Data Sheet (ADS) filed in the USPTO for this case on August 16, 2002 expressly rescinding claim to the benefit of priority under 35 U.S.C. § 120. Applicants respectfully request acknowledgment of this rescission of any priority claim in the present application.

In the Office Action, the Examiner vacated the previous restriction requirement and subjected the claims to a new restriction requirement. The Examiner stated that the claims "disclose a plurality of distinct inventions" (page 2, paragraph 3) and requested "an amendment whereby claims will be modified so to read only upon the elected embodiment" (page 3, paragraph 5).

Applicants wish to thank the Examiner for his comments during a telephone conversation on February 4, 2003, indicating that the restriction requirement required identification of a single sequence for each domain of the novel chimeric phosphorylation indicators.

Applicants hereby provisionally elect, with traverse, the embodiment comprising a polynucleotide encoding a chimeric phosphorylation indicator, where the chimeric phosphorylation indicator comprises, in operative linkage, a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule, wherein said donor molecule comprises ECFP (amino acids 1-227 of SEQ ID NO:6), said

phosphorylatable domain comprises EEEAEYMNMAPQS (SEQ ID NO:23), said phosphoaminoacid binding domain comprises a Src homology domain-2, and said acceptor molecule comprises citrine (YFP; SEQ ID NO:10 having Q69M).

The Examiner asserts in the Office Action that the claims disclose a plurality of distinct inventions. Applicants respectfully submit that all the inventions disclosed in the instant application are related inventions that share the common element of a novel chimeric phosphorylation indicator, and are directed to molecules having a novel structure comprising a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule.

The Examiner asserts in the Office Action that the sequences are patentably distinct because they are unrelated sequences. Applicants respectfully submit that the sequences are related by structure, by functionality, and by utility.

All polynucleotide sequences of the invention are directed to polynucleotides encoding novel chimeric phosphorylation indicators that have the common structural elements (i.e., a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule) recited in original claim 1, in claim 95 added in the previous amendment, and in the specification e.g., at page 3, paragraph 8. The polynucleotides of the invention encode peptide molecules that share common features derived from the fluorescent proteins from which elements of these chimeric polypeptides are derived. Thus, the encoded polypeptides sharing common structural elements, all the claimed polynucleotide sequences are related at least by the structures that they encode.

All the novel phosphorylation indicators encoded by the polynucleotides of the invention can specifically bind a phosphoaminoacid; comprise a donor moiety capable of being excited; can exhibit a detectable resonance energy transfer when the donor is excited; and have domains (i.e., a phosphorylatable domain and a phosphoaminoacid binding domain) that do not substantially emit light to excite the acceptor. Thus, all the nucleic acid sequences of the invention encode novel phosphorylation indicators which share common functions and modes of operation.

All the novel phosphorylation indicators of the invention are suitable for use in detecting a kinase or a phosphatase in a sample; or for detecting the absence of kinase or phosphatase activity in a sample. Thus, they all share common utility.

Thus, for at least the reasons that the phosphorylation indicators of the invention are related by structure, function, modes of operation, and utility, applicants respectfully submit that examination of claims 95-166 as submitted in the previous amendment would not place a serious burden on the Examiner, and would facilitate the expeditious examination of the claimed invention.

Searching the Claims Would Not Pose a Serious Burden on the Examiner

Applicants respectfully submit that different searches are not required in order to search the inventions of claims 95-166. Applicants respectfully submit that the polypeptides encoded by the polynucleotides of the invention are recognized in the art as related subject matter, and do not comprise divergent subject matter that have acquired a separate status in the art. The art recognizes such fluorescent proteins as related, and discusses such related proteins together. For example, a review "The Green Fluorescent Proteins" (Ann. Rev. Biochem. 67:509-544 (1998), by Tsien) discusses the similarities and common uses of different fluorescent proteins related to the ones encoded by the polynucleotides disclosed and claimed in the present application.

Applicants respectfully submit that multiple searches are unnecessary to identify references of relevance to all pending claims. A single search sufficing, no serious burden would be placed on the Examiner. Thus, for at least the reasons that the polynucleotides of the invention are related by structure, function, and utility, applicants respectfully submit that claims 95-166 disclose related inventions that may be searched together without serious burden on the Examiner.

Any Perceived Burden on the Examiner Can Be Reasonably Minimized by an Election of Species Requirement

The pending claims include generic claims that recite polynucleotides encoding chimeric phosphorylation indicators that share common elements, functions and uses. The generic claims are suitably limited in scope, and define those phosphorylation indicator species that find use with the invention.

Applicants believe that additional restriction to recite a single sequence is inappropriate, and such proposed restriction would appear to be more consistent with election of species practice. If this restriction requirement were reassessed and made an election of species requirement, the Applicants would elect a single sequence, and that sequence would be examined only in the event that the broader generic claims were held not to be allowable.

Restriction to a Single Sequence Places a Serious Burden on the Applicant

As discussed above, Applicants respectfully submit that the polynucleotides and the proteins they encode are related, sharing common structural, functional, and useful features despite having different sequences. For example, there are more than a dozen polypeptide species recited in the claims. If the restrictions imposed by the Examiner were proper, Applicant would be required to file no fewer than a dozen patent applications in order to protect polynucleotides encoding these polypeptides. Still more applications would be required to protect the methods of the invention. Applicants respectfully submit that such a large number of applications clearly presents an unreasonable financial burden in obtaining effective patent protection for the invention described in the present application.

Applicants respectfully submit that is unreasonable to assume that an applicant with limited financial resources would file so many applications. For at least this reason, this type of restriction requirement places some Applicants at a disadvantage in protecting their intellectual property. Thus, in the case where an applicant cannot afford the expense of numerous patent applications, the invention is essentially disclosed to the public in its entirety without proper compensation to the applicant in the form of patent protection for the invention.

Restriction to a Single Sequence Differs from Prior USPTO Practice

Applicants respectfully submit that the present requirement to restrict the claims to a single sequence does not follow prior United States Patent and Trademark Office practice, nor is it required by MPEP 803.04 cited by the Examiner. Applicants respectfully note that in other applications submitted by the same inventor, dealing with similar subject matter, a much wider range of sequences has been examined, and broad claims have issued (see, e.g., the recently issued US Patent 6,469,154). Thus, Applicants respectfully submit that the present restriction requirement is in contrast to precedent, and thus, in addition to being unduly limiting, is unnecessary.

Such changes in examination practice not only place an undue burden on applicants, as discussed above, but drastically upset the reasonable expectations of the applicants. As the Examiner is no doubt well aware, a patent application represents a significant investment on the part of the applicant. However, where the extent and value of the patent protection that might be obtained is severely restricted, as occurs, for example, when an application directed to a broad invention representing significant work by the applicant is limited to only a single one of the sequences disclosed in the application, the reasonable expectations of an applicant are confounded.

Restriction to a Single Sequence Violates the Quid Pro Quo Underlying U.S. Patent Law

Applicants respectfully submit that the present requirement to restrict the claims to a single sequence would require the disclosure of Applicant's broad invention without providing patent protection commensurate with that disclosure, inequitably violating the delicate balance between an inventor's disclosure of his invention and the protection afforded by U.S. patent law:

> [T]he patent laws require inventors to describe their work in 'full, clear, concise and exact terms,' 35 U.S.C. § 112, as part of the delicate balance the law attempts to maintain between inventors, who rely on the promise of the law to bring the invention forth, and the public, which should be encouraged to pursue innovations, creations and new ideas beyond the inventor's exclusive rights. *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150 (1989).
>
> Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd. 122 S. Ct. 1831, 62 USPQ2d 1705 (2002)

Restriction of Applicants' claims to a single sequence severely limits the breadth of Applicant's right to exclude others from practicing the invention, while providing the world with the full disclosure of the entire breadth of the invention. Applicants respectfully submit that such a severe restriction is inequitable and unfairly takes advantage of the Applicants' disclosure without providing commensurate rights to exclude in compensation.

CONCLUSION

The Examiner is respectfully requested to reconsider the present restriction requirement in view of the arguments provided herein.

By provisionally electing with traverse, providing arguments herein, and requesting the Examiner to reconsider the restriction requirement, Applicants hereby preserve their right to Petition from the requirement for restriction under 37 C.F.R. § 1.144.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641.

Respectfully submitted,

Dated: March 10, 2003

By: James A Fox
James A. Fox
Registration No. 38,455

Heller, Ehrman White & McAuliffe
275 Middlefield Road
Menlo Park, California 94025-3506
(650) 324-6951 telephone
(650) 324-6654 facsimile

MARKED-UP COPY OF CLAIMS SHOWING CHANGES MADE

95. (Amended) A polynucleotide encoding a chimeric phosphorylation indicator, where the chimeric phosphorylation [indictor] indicator comprises, in operative linkage, a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule,

wherein [the phosphoaminoacid binding domain specifically binds to a phosphoaminoacid when present in the phosphorylatable domain,

wherein the donor molecule and the acceptor molecule exhibit a detectable resonance energy transfer when the donor is excited, and

wherein the phosphorylatable domain and phosphoaminoacid binding domain do not substantially emit light to excite the acceptor] said donor molecule comprises ECFP (amino acids 1-227 of SEQ ID NO:6), said phosphorylatable domain comprises EEEAEYMNMAPQS(SEQ ID NO:23), said phosphoaminoacid binding domain comprises a Src homology domain-2, and said acceptor molecule comprises citrine (YFP; SEQ ID NO:10 having Q69M).

106. (Amended) The polynucleotide of claim [96] 95, wherein [the] at least one of the donor and the acceptor comprises a fluorescent protein which comprises a mutation of an amino acid residue corresponding to positions [A]206, [L]221, [F]223, or a combination thereof of SEQ ID NO:[2] 6 or 10.